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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of Yan Liu, et al	Examiner: J. Ludlow
Serial No.: 09/017,050	Group Art Unit: 1743
Filing Date: 2 February 1998	
For: LARGE CAPACITY ACID OR BASE GENERATION APPARATUS AND METHOD OF USE	

CERTIFICATE OF MAILING

I hereby certify that this correspondence, including listed enclosures, is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, DC 20231 on December 15, 1999 December 17, 1999

Signed: Alison Bowden

Alison Bowden

Assistant Commissioner
for Patents
Washington, D.C. 20231

DECLARATION OF YAN LIU

I, Yan Liu, Ph.D., state and declare as follows:

1. I am a co-inventor of the above application. My education and experience as set forth in Exhibit A attached hereto.

2. I have reviewed the above application and the amendment submitted herewith together with the prior art. In my view, neither Dasgupta nor Anderson alone or in combination disclose the method of the present claims.

3. Referring to Claim 50, a large volume of a cation source reservoir is defined compared to the base generation chamber. This system with a static reservoir is incorporated into a commercial product named EG40 Eluent Generator sold by Dionex Corporation. The device uses a static reservoir with a large volume of a cation source which permits the system to operate continuously for 2,000 hours when the device is used to generate 25 mN KOH at 1.0 ml/min, which is a rather common operating

condition for ion chromatography prior to refilling the solution in the reservoir. This is a far simpler and less expensive system than the one disclosed in Dasgupta which requires an additional pump to pump the sodium hydroxide to the eluent generator and a high pressure chromatography pump. Dasgupta experimented with many different configurations but all of them uses the approach of pumping an acid or base source stream continuously through a flow channel. In my opinion, the large reservoir approach in the present invention provides significant advantages over the continuously flowing solutions in that it is simpler to use and less expensive. In my opinion, this was a significant factor in the commercial success of an eluent generator sold by Dionex Corp. The total revenue of EG40 eluent generator products between April 1, 1998 and December 10, 1999 is about $1.95 million.

4. The use of a higher pressure in the cation source reservoir than in the base generation chamber, as claimed in Claim 51, is not suggested by Dasgupta. Claim 51 is consistent with use of a single pump to be used, as illustrated in Claim 106.

5. In my opinion, the use of a cation exchange bed as the source of the cations as set forth in Claim 52 is not suggested by Dasgupta. He discloses a screen for ion transport but there is a flowing stream source of the cations as set forth above. The use of a cation exchange bed as the source of cations has many advantages such as eliminating Donnan leakage through the membrane since there is no counter ion in solution. The flowing stream approach of Dasgupta can cause problems because the counter ions at the relatively high concentrations could easily leak across the relatively thin ion exchange membranes and contaminate the eluent generated.

6. The disclosed thin membranes of Dasgupta could create significant problems for the embodiment of the present invention in which high pressure is maintained on the acid or base generation side of the membrane. The actual membranes used in the

examples are in the range of 0.05 to 0.1 mm with a maximum disclosed thickness of 0.25 mm. The form of membrane and device is of the type disclosed of Pohl et al U.S. Patent No. 4,999,098 which relates to a suppressor of the type sold commercially by Dionex Corporation. I am familiar with that type of device. In my opinion, the devices disclosed by Dasgupta tend to rupture or leak at pressures greater than about 500 psi because of the use of thin ion exchange membrane.

7. Experiments have been performed at Dionex to determine the effect of varying the thickness of the barrier on the performance of eluent generation devices disclosed in the present application, especially in regard to the ability to withstand high pressure. The results of such experiments are as follows:

Barrier Thickness	Results
0.86 mm	Leakage occurred at 1,000 psi
2.6 mm	Leakage occurred at 2,000 psi
2.7 mm	No leakage at 3,000 psi
1.42 mm	No leakage at 3,500 psi
1.73 mm	Leakage at 2,500 psi
3.36 mm	No leakage at 3,500 psi
4.48 mm	No leakage at 3,500 psi

8. From the above information, leakage is shown at 1,000 psi for a thickness of about 0.86 mm, over three times the maximum thickness disclosed in Dasgupta. , and less than the 1.0 mm thickness of Claim 102.

9. Dasgupta does not disclose pressure maintenance in the base generation chamber of at least 50 psi as set forth in Claim 99. Such pressures are typical for high performance liquid chromatography.

10. The thin barriers of Dasgupta could create serious Donnan leakage problems

particularly for the use of a salt as the cation or anion source. The anion component of the salt tends to leak through a membrane as thin as disclosed the Dasgupta patent which can create significant interference with the analysis in which the eluent generation devices are used.

11. Dasgupta does not recite that the aqueous liquid stream is pumped through the first base generation chamber using a pump with an outlet disposed upstream of the base generation chamber as shown in Claim 106. This permits the use of a single pump to pump the aqueous liquid stream through the base generator and through the chromatography column, making the system much less expensive than the Dasgupta system. Moreover, water rather generated acid or base flows through the pump significantly increasing its lifetime. Further, the pump has dead volume which can create error and particularly the use of gradient eluents. The source of error is eliminated in the method of Claim 106 in which the pump is upstream of the eluent generator because the base generation chamber of the base generators disclosed in the present invention has significantly smaller dead volume(50 to 150 μL). In contrast, a typical pump has a dead volume of 1,000 to 2,000 μL.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application and any patent issuing therefrom.

Date: 12-15-1999 Yan Liu

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SUMMARY OF PROFESSIONAL EXPERIENCE

Sixteen years of experience as an analytical chemist devoted to the research, development, and validation of new technologies, instrumentation, and methods and for chemical analysis. Author and co-author of 25 publications in peer-reviewed technical journals and 24 presentations at national and international technical conferences. Areas of specialization include:

- Development of novel analytical instrumentation in the field of chromatography
- Development and validation of analytical methods
- Separation techniques (IC, GC, HPLC, CE, and SFC)
- Design and use of devices based on electrically polarized ion exchange materials
- Spectroscopic techniques (AA, ICP-MS, ICP-AES, MS, IR)
- Sample preparation techniques (SFE, SPE, ion exchange resins, wet chemical methods)
- Microcontaminant analysis for semiconductor and microelectronics devices
- Materials characterization by chemical analysis
- Gas chromatography with atomic emission detection
- Trace metal analysis, complexation, and speciation
- Determination of organometallic compounds

EDUCATION

Ph.D., Analytical Chemistry, Oregon State University, 1987
B.S., Analytical Chemistry, Xiamen University, 1982

PROFESSIONAL EXPERIENCE

Staff Research Chemist, Dionex Corporation, Sunnyvale, California, 11/95-present
Served as principal investigator and project leader in research projects that focus on the development of novel instrumentation and methodology in the field of chromatography. Representative project experience includes:

- Development of novel devices based on electrically polarized ion exchange beds for generation and recycle of acid, base, and salt solutions for use as eluents in ion chromatography.

- Development of an automated on-line acid and base generation system (EG40) for ion chromatography.

- Development of high performance anion exchange chromatography/pulsed electrochemical detection method for direct and sensitive detection of amino acids.

Principal Chemist, Midwest Research Institute, California Operations, Mountain View, California, 4/92-11/95

Served as principal investigator and project leader in contract research and method development projects. Project management duties included business development through effective marketing strategies, preparation of competitive technical proposals and project budgets, supervision of 2 to 3 chemists, and successful leadership in various projects performed for industrial and government clients. Representative project experience included:

- Development of analytical method for the determination of trace contaminants (i.e, organotin compounds, inorganic anions, etc.) in semiconductor and microelectronics devices.
- Development and validation of analytical method for the determination of haloacetic acids in drinking water using ion chromatography.
- Development of a novel interface to couple capillary zone electrophoresis to inductively coupled plasma/mass spectrometry for trace metal speciation.
- Development of an off-line SFE and GC with atomic emission detection methods for determination of organotin, organolead, and organomercury compounds in solid samples.
- Development of in situ complexation/SFE technique for extraction of toxic metals such as Cr(III), Cr(VI), Hg(II), Cd(II), and Pb(II) from solid samples.
- Development of a high-performance centrifugal partition chromatography technique for extraction of organic compounds such as phenols and organochlorine pesticides from aqueous samples.
- Development of a novel interface to couple capillary zone electrophoresis to microwave-induced helium plasma atomic emission detector.
- Development of an ultrasound-SFE technique for extraction of organic compounds from environmental samples.

Senior Research Chemist, Dionex Corporation, Sunnyvale, California, 1988-1992

Worked as a principal investigator in different analytical instrumentation and method development projects. The representative experience included:

- Conducted research in the area of capillary electrophoresis, including the development of

gel- filled and coated capillary columns for CE.

- Researched and developed instrumentation and methods in the area of microcolumn unified chromatography, including GC, SFC, and LC.
- Researched and developed packed microbore SFC columns with polymer stationary phases for the analysis of polar organic compounds in environmental samples.
- Worked on technical marketing support for applications of IC in environmental analysis.
- Researched and developed automated online photodissociation/gas diffusion membrane separation/IC system for cyanide analysis.

Postdoctoral Associate, Department of Chemistry, University of California, Riverside, California, 1987-1988

Conducted research in the area of combined GC/IR/MS analysis of organic compounds and applications of IR, MS, and NMR spectral and structural data bases in computer-assisted identification of organic compounds.

Research/Teaching Assistant, Department of Chemistry, Oregon State University, Corvallis, Oregon, 1983-1987

Conducted research in the area of trace metal analysis and studied trace metal complexation and speciation. Researched and developed automated online ion exchange chromatography/flame atomic absorption detection systems for determining trace metal speciation and complexation in natural waters. Worked as laboratory instructor for undergraduate and graduate courses in spectrochemical analysis, microcomputer programming and interfacing, quantitative analysis, and general chemistry.

PROFESSIONAL AFFILIATIONS AND ACTIVITIES

- American Chemical Society
- American Water Works Association
- California Separation Science Society
- Bay Area Mass Spectrometry Society
- Phi Lambda Upsilon (chemistry honor society)

PROFESSIONAL DEVELOPMENT

- Semiconductor Fabrication Technology, University of California, 1995
- Inductively Coupled Plasma-Mass Spectrometry (ICP-MS), Pittsburgh Conference, 1995
- Internet Basics, Foothill College, 1995
- Project Management, University of California, 1993
- Managing a Winning Proposal, University of California, 1993

- Technical Writing, University of California, 1992

PUBLICATIONS

1. Liu, Y., and J. D. Ingle, Jr., "Measurement and Compensation for Metal Complex Dissociation in Speciation Studies with an Automated Two-column Ion Exchange System," *Analytica Chimica Acta*, 222, 279-289 (1989).

2. Liu, Y., and J. D. Ingle, Jr., "Two-column Ion Exchange Method for the Determination of Copper Complexing Capacity and Conditional Stability Constants of Copper Complexes for Ligands in Natural Waters," *Talanta*, 36, 185-192 (1989).

3. Liu, Y., and J. D. Ingle, "Automated Two-column Ion Exchange System for Determination of the Speciation of Trace Metals in Natural Waters," *Analytical Chemistry*, 61, 525-529 (1989).

4. Liu, Y., and J. D. Ingle, Jr., "Automated On-Line Ion exchange Trace Enrichment System with Flame Atomic Absorption Detection," *Analytical Chemistry*, 61, 520-524 (1989).

5. Liu, Y., R. D. Rocklin, R. J. Joyce, and M.J. Doyle, "Photodissociation/Gas Diffusion/Ion Chromatography System for Determination of Total and Labile Cyanide in Waters," *Analytical Chemistry*, 62, 766-770 (1990).

6. Liu, Y., F. J. Yang, and C. Pohl, "Microbore Packed Column Supercritical Fluid Chromatography with a New Polymer Stationary Phase," *Journal of Microcolumn Separations*, 2, 245-254 (1990).

7. Liu, Y., and F. J. Yang, "High Pressure Microbore Packed Column Gas Chromatography Using Common Liquid Chromatography Stationary Phases," *Journal of Microcolumn Separations*, 3, 249-257 (1991).

8. Liu, Y., and F. J. Yang, "Unified High Pressure Gas and Supercritical Fluid Chromatography with Microbore Packed Columns," *Analytical Chemistry*, 63, 926-930 (1991).

9. Liu, Y., V. Lopez-Avila, M. Alcaraz, and W. F. Beckert, "Determination of Organotin Compounds in Environmental Samples by Supercritical Fluid Extraction and Gas Chromatography with Atomic Emission Detection," *Journal of High Resolution Chromatography*, 16, 106-112 (1993).

10. Liu, Y., V. Lopez-Avila, M. Alcaraz, W. F. Beckert, and E. M. Heithmar, "Determination of Metals in Solid Samples by Complexation/Supercritical Fluid Extraction and Gas Chromatography—Atomic Emission Detection," *Journal of Chromatographic Science*, 31, 310-316 (1993).

11. Liu, Y., and V. Lopez-Avila, "On-line Microwave-Induced Helium Plasma Atomic Emission Detection for Capillary Zone Electrophoresis," *Journal of High Resolution Chromatography*,

16,717-720 (1993).

12. Lopez-Avila, V., Y. Liu, and M. Alcaraz, "Feasibility of Applying Ultrasound During Supercritical Fluid Extraction," U.S. EPA Publication No. EPA/600/X-94-001, March, 1994.

13. Liu, Y., V. Lopez-Avila, and M. Alcaraz, "Off-line Complexation/Supercritical Fluid Extraction and Gas Chromatography with Atomic Emission Detection for the Determination of Organotin, Organolead, and Organomercury Compounds in Soils and Sediments," U. S. EPA Publication No. EPA/600/R1-94/00X, April, 1994.

14. Liu, Y., V. Lopez-Avila, M. Alcaraz, and W. F. Beckert, "Simultaneous Determination of Organotin, Organolead, and Organomercury Compounds in Environmental Samples Using Capillary Gas Chromatography with Atomic Emission Detection," *Journal of High Resolution Chromatography*, 17, 527-536 (1994).

15. Liu, Y., V. Lopez-Avila, M. Alcaraz, and W. F. Beckert, "Off-line Complexation/Supercritical Fluid Extraction and Gas Chromatography with Atomic Emission Detection for Determination of Organotin Compounds in Soils and Sediments," *Analytical Chemistry*, 66, 3788-3796 (1994).

16. Liu, Y., V. Lopez-Avila, M. Alcaraz, and T. Jones, "Centrifugal Partition Chromatographic Extraction of Phenols and Organochlorine Pesticides from Aqueous Samples," *Analytical Chemistry*, 66, 4483-4489 (1994).

17. Liu, Y., V. Lopez-Avila, J. Zhu, D. Wiederin, and W. F. Beckert, "Capillary Electrophoresis Coupled with On-line Inductively-Coupled Plasma Mass Spectrometric Detection", *Analytical Chemistry*, 67, 2020-2025 (1995).

18. Liu, Y., V. Lopez-Avila, M. Alcaraz, and W. F. Beckert, "Interlaboratory Study of A Capillary Gas Chromatography/Atomic Emission Detection Method for Determination of Organotin Compounds", *AOAC International*, (1995), in press.

19. Wai, C. M., S. Wang, Y. Liu, V. Lopez-Avila, and W. F. Beckert, "Evaluation of Dithiocarbamates and β-Diketones as Chelating Agents in Supercritical Fluid Extraction of Cd^{2+}, Pb^{2+}, and Hg^{2+} ions from Solid Samples", *Talanta*, 43, 2083-2091 (1995).

20. Lopez-Avila, V., Y. Liu, and C. Charan, "Development of an Ion Chromatography Method for the Determination of Haloacetic Acids in Water", *AOAC International*, (1998), in press

21. Liu, Y. N. Avdalovic, C. Pohl, R. Matt, H. Dhillon, R. Kiser, "An On-Line, High-Purity Acid and Base Eluent Generation System for Ion Chromatography", *American Laboratory*, November issue, 48C-54C (1998).

22. Small, H., Y. Liu, and N. Avdalovic, "Electrically Polarized Ion Exchange Beds in Ion Chromatography: Eluent Generation and Recycle", *Analytical Chemistry*, 70, 3629-3635 (1998).

23. Clark, A. P., P. Jandik, R. D. Rocklin, Y. Liu, and N. Avdalovic, "An Integrated

Amperometry Waveform for the Direct, Sensitive Detection of Amino Acids and Amino Sugars Following Anion-Exchange Chromatography", *Analytical Chemistry*, 71, 2774-2781 (1999).

24. Liu, Y., E. Kaiser, and N. Avdalovic, "Determination of Trace-Level Anions in High-Purity Water Samples by Ion Chromatography with an Automated On-Line Eluent Generation System", *Microchemical Journal*, 62, 164-173 (1999).

25. Kiser, R. , Y. Liu, and D. Jensen, "On-line generation of Acid and Base Eluents for Ion Chromatography", *G. I. Laboratory Journal*, Issue 2, (1999), in press.

PRESENTATIONS AT NATIONAL AND INTERNATIONAL MEETINGS

1. Liu, Y., and J. D. Ingle, Jr., "Automated Ion Exchange Systems for the Determination of Chemical Speciation of Trace Metals in Natural Waters," Presented at the 42nd Northwest ACS Meeting (June 1987).

2. Liu, Y., "Automated Two-column Ion Exchange Method for the Determination of Cu(II) Complexing Capacity and Conditional Stability Constants of Ligands in Natural Waters," Presented at the 196th ACS National Meeting (September 1988).

3. Liu, Y., M. Doyle, and R. J. Joyce, "Determination of Total Cyanide Utilizing On-line Photodissociation of Metal Cyanide Complexes," Presented at the Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy (March 1989).

4. Liu, Y., and R. Rocklin, "Determination of Free and Total Cyanide Using On-line UV Photodissociation of Metal Cyanide Complexes," Presented at the 6th Symposium on Ion Chromatography, Switzerland (April 1989).

5. Liu, Y., R. J. Joyce, and R. Rocklin, "Automated On-line Photodissociation/Gas Diffusion Membrane Separation/Ion Chromatography Method for Determination of Total Cyanide in Wastewaters," Presented at the Rocky Mountain Conference on Analytical Chemistry (October 1989).

6. Liu, Y., and R. J. Joyce, "Automated Determination of Free and Total Cyanide in Waste Water Using Photodissociation and Gas Dialysis Followed by Ion Chromatographic Determination," Presented at the Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy (March 1990).

7. Liu, Y., C. Pohl, and F. Yang, "Advance New Polymeric Packing Material for Microbore Packed Column Supercritical Fluid Chromatography," Presented at the Pittsburgh Conference on Analytical Chemistry and Supplied Spectroscopy (March 1990).

8. Liu, Y., C. Pohl, F. Yang, "A Universal Microbore Packed Column for GC, SFC, LC, and IC," Presented at the Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy (March 1990).

9. Liu, Y., and F.J. Yang, "Microparticulate Polymer Packed Microcolumns for GC, SFC, LC, and IC," Presented at the 2nd International Symposium and Workshop on Microcolumn Separation Methods, Sweden (September 1990).

10. Liu, Y., V. Lopez-Avila, and W. F. Beckert, "Determination of Organometallic Compounds in Environmental Samples by Supercritical Fluid Extraction and Gas Chromatography with Atomic Emission Detection," Presented at the Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, Atlanta, Georgia (March 1993).

11. Liu, Y., V. Lopez-Avila, and W. F. Beckert, "In Situ Complexation and Supercritical Fluid Extraction of Trace Metals from Environmental Samples," Presented at the Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, Atlanta, Georgia (March 1993).

12. Liu, Y., V. Lopez-Avila, and W. F. Beckert, "Combination of SFE with Capillary GC and Atomic Emission Detection for Determination of Organotin Compounds in Environmental Samples," Presented at the 16th Annual EPA Conference on Analysis of Pollutants in the Environment, Norfolk, Virginia (May 1993).

13. Liu, Y. V. Lopez-Avila, C. Charan, M. Alcaraz, and W. F. Beckert, "Application of Supercritical Fluid Extraction to Speciate Mercury Compounds in Soil and Sediment Samples," Presented at the 5th International Symposium on Supercritical Fluid Chromatography and Extraction, Baltimore, Maryland (January 1994).

14. Liu, Y., V. Lopez-Avila, M. Alcaraz, and W. F. Beckert, "Off-Line SFE and GC/AED Method for Organotin Compounds in Environmental Samples," Presented at the 5th International Symposium on Supercritical Fluid Chromatography and Extraction, Baltimore, Maryland (January 1994).

15. Liu, Y., and V. Lopez-Avila, "On-Line Microwave-Induced Helium Plasma Atomic Emission Detection for Capillary Zone Electrophoresis," Presented at the 6th International Symposium on Symposium on High Performance Capillary Electrophoresis, San Diego, California (January 1994).

16. Liu, Y., and V. Lopez-Avila, M. Alcaraz, W. F. Beckert, and C. M. Wai, "Complexation/Supercritical Fluid Extraction of Metal Ions from Environmental Solid Samples," Presented at the 45th Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, Chicago, Illinois (February 1994).

17. Liu, Y., V. Lopez-Avila, M. Alcaraz, and W. F. Beckert, "Determination of Organotin and Organolead Compounds in Environmental Samples by Off-Line Supercritical Fluid Extraction and Capillary Gas Chromatography with Atomic Emission Detection," Presented at the 45th Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, Chicago, Illinois (February 1994).

18. Liu, Y. "Determination of Organometallic Compounds in Environmental Solid Samples by Off-

Line SFE and Capillary GC with Atomic Emission Detection," Presented at Advanced Laboratory Exposition and Conference/West, San Jose, California (October 1994).

19. Liu, Y., V.Lopez-Avila, R. Joyce, J. Stillian, and E. Kaiser, "Development of an Improved and Direct Method for the Detection of Haloacetic Acids in Drinking Water," Presented at the 46th Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, New orleans, Louisiana (March 1995).

20. Liu, Y., V. Lopez-Avila, M. Alcaraz, and W. F. Beckert, "Interlaboratory Evaluation of a SFE and a GC-AED Method for the Determination and Speciation of Organotin Compounds in Soil and Sediment Samples," Presented at the 46th Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, New orleans, Louisiana (March 1995).

21. Liu, Y., V. Lopez-Avila, J. J. Zhu, and W. F. Beckert, "CE Coupled On-line with Inductively Coupled Plasma Mass Spectrometry for Elemental Speciation,", Presented at the 17th International Symposium on Capillary Chromatography and Electrophoresis, Wintergreen, Virginia (May 1995).

22. Liu, Y., N. Avdalovic, H. Small, R. Matt, and H. Dhillon, "On-line Large capacity High Purity Acid and Base Generation Devices and Their Applications in Ion Chromatography", Presented at the 46th Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, New orleans, Louisiana (March 1998).

23. Liu, Y., N. Avdalovic, J. Rohrer, M. Laikhtman, E. Kaiser, and H. Dhillon, "Determination of Trace-Level Anions in High-Purity Water by Ion Chromatography with On-Line Eluent Generation", Presented at 1998 International Ion Chromatography Symposium, Osaka, Japan (September 1998).

24. Liu, Y., N. Avdalovic, J. Rohrer, M. Laikhtman, E. Kaiser, and H. Dhillon, "Determination of Trace-Level Anions in High-Purity Water by Ion Chromatography with On-Line Eluent Generation", Presented at 1998 International Ion Chromatography Symposium, Osaka, Japan (September 1998).